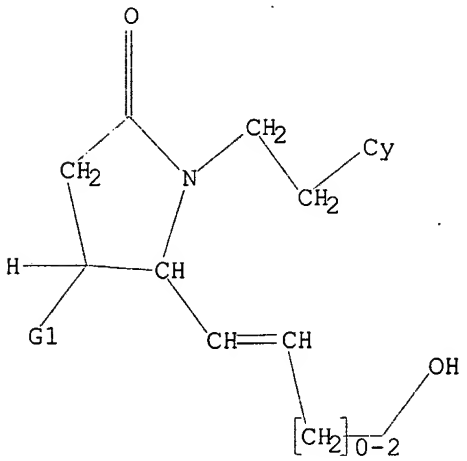
L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



G1 H,OH

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
FULL SEARCH INITIATED 11:31:17 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1759 TO ITERATE

100.0% PROCESSED 1759 ITERATIONS 134 ANSWERS
SEARCH TIME: 00.00.01

L2 134 SEA SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	166.94	167.15

FILE 'CAPLUS' ENTERED AT 11:31:23 ON 08 DEC 2006
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FILE COVERS 1907 - 8 Dec 2006 VOL 145 ISS 25
FILE LAST UPDATED: 7 Dec 2006 (20061207/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
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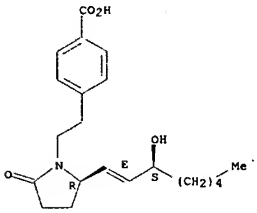
=> s l2
L3 7 L2

=> d ibib abs hitstr 1-7

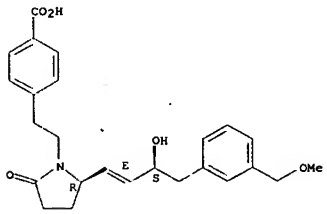
L3 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:956785 CAPLUS
DOCUMENT NUMBER: 142:85862
TITLE: Lactams as EP4 Prostanoid Receptor Agonists. 3. Discovery of N-Ethylbenzoic Acid 2-Pyrrolidinones as Subtype Selective Agents
AUTHOR(S): Elworthy, Todd R.; Brill, Emma R.; Chiou, San-San; Chu, Frances; Harris, Jason R.; Hendricks, R. Than; Huang, Jane; Kim, Woongki; Lach, Leang K.; Mirzadegan, Tara; Yee, Calvin; Walker, Keith A. M.
CORPORATE SOURCE: Roche Palo Alto, Palo Alto, CA, 94304, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(25), 6124-6127
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:85862
AB Two distinct synthetic schemes were applied to access heteroatom-containing α-chain lactams or lactams terminated as aryl acids. The latter lactams were devised using a pharmacophore for EP4 receptor activity. γ-Lactams were characterized for their prostanoid EP receptor affinities and EP4 activity and found to be selective for the EP2 and EP4 receptors or selective for the EP4 subtype. Benzoic acid 17 displayed enhanced in vivo exposure relative to 3.
IT 493036-24-1P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(discovery of N-ethylbenzoic acid 2-pyrrolidinones as EP4 prostanoid receptor agonists)
RN 493036-24-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L3 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

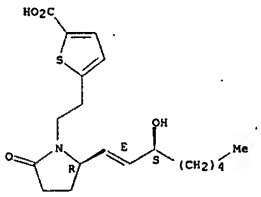


REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

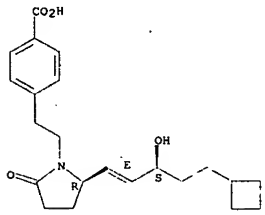
IT 493036-36-5P 819067-18-0P 819067-20-4P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(discovery of N-ethylbenzoic acid 2-pyrrolidinones as EP4 prostanoid receptor agonists)
RN 493036-36-5 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 819067-18-0 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-5-cyclobutyl-3-hydroxy-1-pentenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 819067-20-4 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-[3-(methoxymethyl)phenyl]-

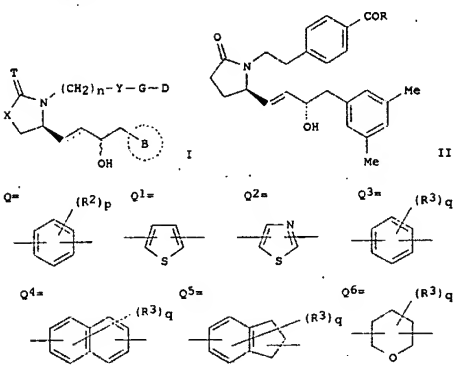
L3 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:633912 CAPLUS
DOCUMENT NUMBER: 141:156958
TITLE: Preparation of 8-azaprostaglandin derivatives as prostaglandin EP4 receptor agonists
INVENTOR(S): Kambe, Tohru; Maruyama, Toru; Kobayashi, Kaoru; Tani, Kousuke; Nakai, Yoshihiko; Nagase, Toshihiko; Maruyama, Takayuki; Sakata, Kiyoto; Yoshida, Hideyuki; Fujimura, Shinsei; Nishiura, Akio; Abe, Nobutaka
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004065365	A1	20040805	WO 2004-JP419	20040120
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ				
JP 2005104836	A2	20050421	JP 2003-289954	20030808
EP 1586564	A1	20051019	EP 2004-703518	20040120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: JP 2003-11936 A 20030121
JP 2003-289954 A 20030808
WO 2004-JP419 W 20040120

OTHER SOURCE(S): MARPAT 141:156958
GI

L3 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

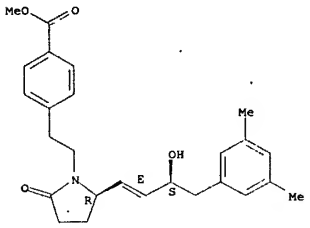


AB Compds. having an 8-azaprostaglandin skeleton represented by the following general formula (I), salts thereof, solvates thereof, clathrate compds. thereof in cyclodextrin, or prodrugs thereof [wherein a solid line accompanied by a dotted line represents a single or double bond; a wavy line for the OH group represents an α- or β-disposition or a mixture with any α/β ratio thereof; D = C1-4 alkoxy-carbonyl, tetrazolyl; the ring A = Q, Q1, Q2; R2 = halo, C1-4 alkyl, C1-4 alkoxy; p = an integer of 0-4; Y = a bond, S; T = O, S; X = CH2, O, S; ring B = Q3, Q4, Q5, Q6; R3 = halo, each mono- to pentahalo-C1-4 alkyl or -C1-4 alkoxy, C1-4 alkoxy-C1-4 alkyl, Ph, each (un)substituted Ph or 3- to-13-membered bi- or tricyclic heterocyclyl containing 1-4 heteroatoms selected from N and S; q = an integer of 0-5] are prepared These compds. are prostaglandin EP4 receptor agonists and thereby useful in preventing and/or treating EP4-mediated diseases such as immune diseases, asthma, nerve cell death, arthritis, pulmonary injury, pulmonary fibrosis, pulmonary emphysema, bronchitis, chronic obstructive pulmonary disease, liver injury, acute hepatitis, nephritis, renal failure, hypertension, myocardial ischemia, systemic inflammatory reaction syndrome, sepsis, hemophagous syndrome, macrophage activation syndrome, Still's disease, Kawasaki's disease, burn, systemic granuloma, ulcerative colitis, Crohn's disease, hypercytokinemia in dialysis, multiorgan failure, shock and glaucoma. Because of having an effect of promoting osteogenesis, moreover, they are useful in preventing and/or treating diseases with bone loss (bone diseases such as primary osteoporosis, secondary osteoporosis, bone metastasis of cancer, hypercalcemia, Behcet's disease, bone defect and bone necrosis, postoperative osteogenesis, alternative therapy for bone transplantation). Thus, (4R,5E,7S)-4-amino-7-hydroxy-8-(3,5-dimethylphenyl)oct-5-enoic acid Et ester hydrochloride (prepn. given) underwent reductive alkylation and cyclization with Me 4-formylmethylbenzoate using sodium triacetoxyborohydride in THF at room temp. overnight to give 2,3,4,5,17,18,19,20-octanor-8-azaprost-13-enoic acid Me ester deriv. (II; R = OMe) which was sapond. by a mixt. of 2 N aq. NaOH soln. and acidified with 2 N aq. HCl soln. to give II (R = OH). II (R = OH) showed the binding activity to prostaglandin EP4 receptor expressed by CHO cells with Ki of 6.4 nM. A tablet and vial formulation contg. a specific compd. I were described.

IT 729611-00-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 8-azaprostaglandin derivs. as prostaglandin EP4 receptor agonists or osteogenesis promoters for preventing and/or treating EP4-mediated diseases or bone diseases)

RN 729611-00-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-(3,5-dimethylphenyl)-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

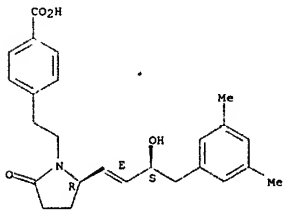
Absolute stereochemistry.
Double bond geometry as shown.



IT 729611-01-2P 729611-02-3P 729611-03-4P
729611-05-6P 729611-07-8P 729611-08-9P
729611-10-3P 729611-11-4P 729611-14-7P
729611-17-0P 729611-18-1P 729611-20-5P
729611-21-6P 729611-22-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 8-azaprostaglandin derivs. as prostaglandin EP4 receptor agonists or osteogenesis promoters for preventing and/or treating EP4-mediated diseases or bone diseases)

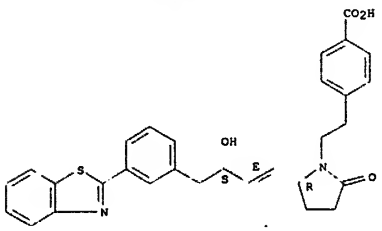
RN 729611-01-2 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-(3,5-dimethylphenyl)-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 729611-02-3 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-[3-(2-benzothiazolyl)phenyl]-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

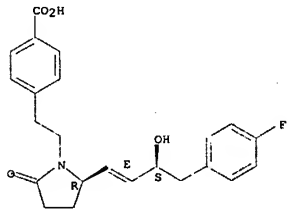
Absolute stereochemistry.
Double bond geometry as shown.



RN 729611-03-4 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

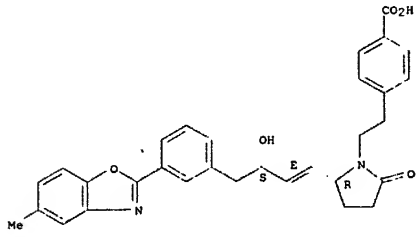
L3 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.
Double bond geometry as shown.



RN 729611-05-6 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-[3-(5-methyl-2-benzoxazolyl)phenyl]-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

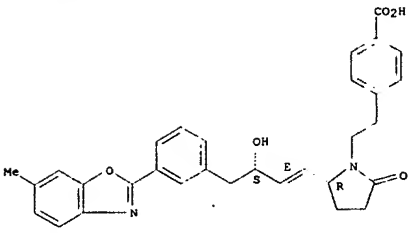
Absolute stereochemistry.
Double bond geometry as shown.



RN 729611-07-8 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-[3-(6-methyl-2-benzoxazolyl)phenyl]-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

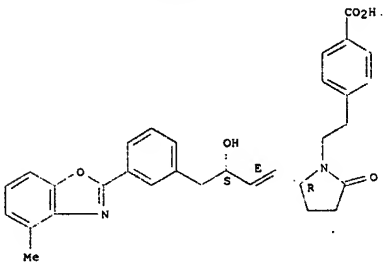
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 729611-08-9 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-[3-(4-methyl-2-benzoxazolyl)phenyl]-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

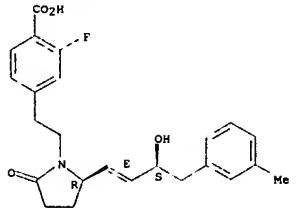
Absolute stereochemistry.
Double bond geometry as shown.



RN 729611-10-3 CAPLUS
CN Benzoic acid, 2-fluoro-4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-methylphenyl)-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

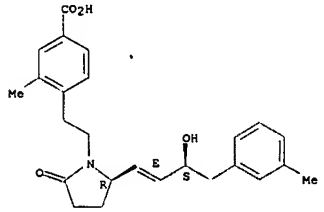
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 729611-11-4 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-methylphenyl)-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]-3-methyl- (9CI) (CA INDEX NAME)

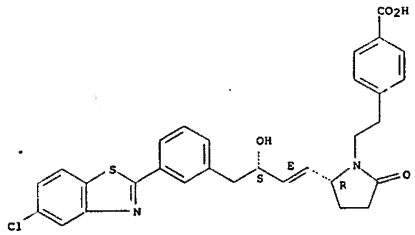
Absolute stereochemistry.
Double bond geometry as shown.



RN 729611-14-7 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-[3-(5-chloro-2-benzothiazolyl)phenyl]-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

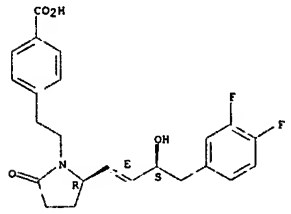
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 729611-17-0 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-(3,4-difluorophenyl)-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

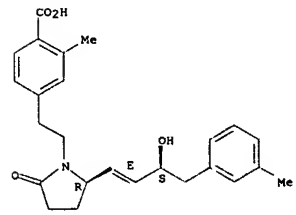
Absolute stereochemistry.
Double bond geometry as shown.



RN 729611-18-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-methylphenyl)-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

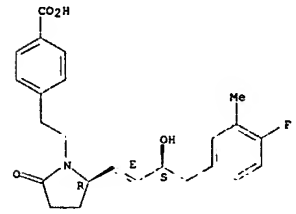
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 729611-20-5 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-(4-fluoro-3-methylphenyl)-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

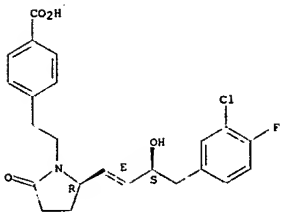
Absolute stereochemistry.
Double bond geometry as shown.



RN 729611-21-6 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-(3-chloro-4-fluorophenyl)-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

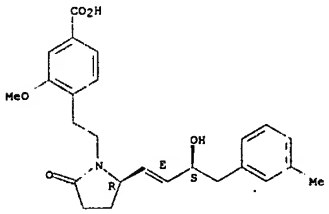
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 729611-22-7 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-methylphenyl)-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]-3-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:370901 CAPLUS
DOCUMENT NUMBER: 140:391154
TITLE: A preparation of pyrrolidinone derivatives useful as selective EP4 receptor agonists
INVENTOR(S): Billot, Xavier; Beunard, Jean-Luc; Han, Yongxin; Young, Robert N.; Colucci, John; Girard, Mario; Wilson, Marie-Claire
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037786	A2	20040506	WO 2003-CA1620	20031023
WO 2004037786	A3	20040930		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2502914	AA	20040506	CA 2003-2502914	20031023
AU 2003275840	A1	20040513	AU 2003-275840	20031023
EP 1558602	A2	20050803	EP 2003-809227	20031023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006505572	T2	20060216	JP 2004-545645	20031023
US 2006167081	A1	20060727	US 2005-528419	20050317
PRIORITY APPLN. INFO.:			US 2002-421402P	P 20021025
			WO 2003-CA1620	W 20031023

OTHER SOURCE(S): MARPAT 140:391154
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

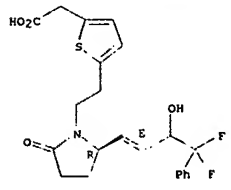
AB The invention relates to pyrrolidinone derivs. of formula I [wherein: Y1 = (CH2)2, CH:CH, 1,2-cyclopropanediyl; Y is C(O) or CH(OH); A is (CH2)1-4; Z = O, S, 1,2-cyclopropanediyl, HC:CH, C.tplbond.C, or a bond; Q is a disubstituted (hetero)aryl ring; W is a bond, unsubstituted C1-6 alkylene,

L3 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
or C1-6 alkylene substituted with 1-4 halogen atoms; R1 = OH, CN, CHO, etc.; R2 = C1-6alkyl, (CH2)0-8-(C6-10aryl), O-C1-10alkyl, etc.; R3 and R4 are independently selected from halogen, C1-6alkyl, or R3 and R4, together with the carbon atom to which they are attached, form a C3-7 cycloalkyl ring] useful as potent selective agonists of the EP4 subtype of prostaglandin E2 receptors. The invention compds. are useful in treatment of glaucoma and other conditions which are related to the elevated intraocular pressure in the eye. The invention relates to the use of the invention compds. for mediating the bone modeling and remodeling processes of the osteoblasts and osteoclasts. The invention compds. were tested as EP4 agonists on intraocular pressure in rabbits and monkeys; prostanoid receptor binding assays and bone resorption assays were performed (in a subclass of the invented compds., agonists have EC50 values from 0.01 μM to 10 μM). The synthesized stereoisomeric pyrrolidinones II were prepd. from pyrrole deriv. III via oxidn., condensation with PhCF2C(O)CH2P(O)(OMe)2, keto-group redn. of the obtained unsatd. ketone IV, alc. protection, N-cleavage, addn. of thiophene deriv. V to the obtained compd. VI, sepn. of the isomers, alc. deprotection, and hydrolysis.

IT 685896-10-0P 685896-11-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidinone derivs. useful as selective EP4 receptor agonists)

RN 685896-10-0 CAPLUS
CN 2-Thiopheneacetic acid, 5-[2-[(2R)-2-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

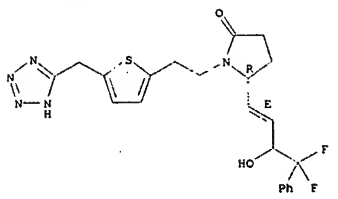
Absolute stereochemistry.
Double bond geometry as shown.



RN 685896-11-1 CAPLUS
CN 2-Pyrrolidinone, 5-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-1-[2-[5-(1H-tetrazol-5-ylmethyl)-2-thienyl]ethyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:991301 CAPLUS
DOCUMENT NUMBER: 140:42024
TITLE: Preparation of γ-lactams as prostaglandin EP4 agonists and uses thereof
INVENTOR(S): Araldi, Gian Luca; Reddy, Adulla P.; Zhao, Zhong; Mckenna, Sean D.; Bao, Bagna
PATENT ASSIGNEE(S): Applied Research Systems Ars Holding N.V, Neth. Antilles
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

Instant App

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003103604	A2	20031218	WO 2003-US18202	20030609
WO 2003103604	A3	20040212		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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CA 2483555	AA	20031218	CA 2003-2483555	20030609
AU 2003237520	A1	20031222	AU 2003-237520	20030609
EP 1556347	A2	20050727	EP 2003-736967	20030609
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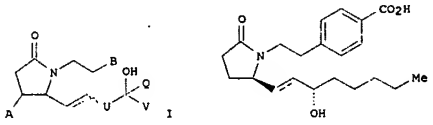
JP 2005533043	T2	20051104	JP 2004-510725	20030609
US 2005288357	A1	20051229	US 2005-517626	20050728
PRIORITY APPLN. INFO.:			US 2002-387340P P	20020610
			US 2003-451804P P	20030303
			WO 2003-US18202 W	20030609

OTHER SOURCE(S): MARPAT 140:42024
GI



L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

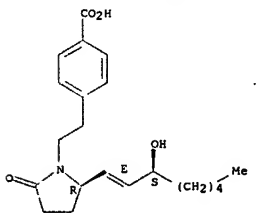
AB Title 1,2-substituted 5-pyrrolidinones I [wherein A = H or OH; B = (un)substituted carbocyclyl, heterocyclyl, or heteroaryl; U = (CH2)p; V and Q = independently H, heteroalkyl, (hetero)cycloalkylalkyl, arylalkyl, CR1R2W, or (un)substituted alkyl, alkenyl, or alkynyl; W = H, alkyl, cycloalkyl(alkyl), or (hetero)aryl; R1 and R2 = independently H or alkyl; or CR1R2 = cycloalkyl; p = 0-2; with the proviso that at least one of V and Q is other than H; and pharmaceutically acceptable salts and prodrugs thereof] were prepared as prostaglandin EP4 receptor agonists. For example,
reaction of H-D-Glu(OBu-t)-OBu-t with 4-carbomethoxyphenylacetaldehyde in the presence of NaCNBH3 in THF afforded tert-Bu 1-[2-[4-(methoxycarbonyl)phenyl]ethyl]-5-oxo-D-prolinate (75%), which was converted to the proline derivative (98%) using TFA. Treatment with N-methylmorpholine and iso-Bu chloroformate, followed by NaBH4, in THF provided Me 4-[2-[(2R)-2-(hydroxymethyl)-5-oxopyrrolidin-1-yl]ethyl]benzoate (50%). Oxidation with oxalyl chloride in DCM gave the aldehyde (97%), which was condensed with di-Me (2-oxoheptyl)phosphonate in
the presence of NaH in THF to provide the 3-oxooct-1-enyl derivative (90%).
Reduction of the ketone to the alc. with NaBH4 in EtOH gave a mixture of two
diastereomeric esters (90%), which were saponified and separated by RP-HPLC
affording (3S)-II and (3R)-II. Compds. of the invention showed selectivity for binding to the human prostaglandin EP4 receptor over the EP2 receptor. For instance, (3S)-II inhibited EP4 and EP2 receptors with Ki values of 2 nM and 120 nM, resp. Administration of (3S)-II triggered ovulation in CD-mice with ED50 values of 3.9 mg/kg s.c, 21.97 mg/kg p.o. in non-fasted animals, and 21.1 mg/kg p.o. in fasted animals. Thus, I and
their pharmaceutical compns. are useful for a variety of therapies, including treating or preventing preterm labor, dysmenorrhea, asthma, hypertension, infertility or fertility disorder, undesired blood clotting,
preeclampsia or eclampsia, an eosinophil disorder, sexual dysfunction, osteoporosis and other destructive bone disease or disorder, renal dysfunction, an immune deficiency disorder, dry eye, ichthyosis, elevated intraocular pressure, sleep disorder, or gastric ulcer, inflammatory disorders, and other diseases and disorders associated with the prostaglandin
family of compds. (no data).

IT 493036-24-1P, 4-[2-[(2R)-2-((1E,3S)-3-Hydroxyoct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(EP4 agonist; preparation of pyrrolidinones as prostaglandin EP4 agonists
for treatment of preterm labor, dysmenorrhea, sexual dysfunction, bone loss, inflammation, and other disorders)

RN 493036-24-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-octenyl]-5-oxo-1-

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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514/424

IT 494223-72-2P, 4-[2-[(2R)-2-[(1E,3S)-3-Hydroxy-4-(3-methylphenyl)but-1-enyl]-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635309-88-5P, 4-[2-[(2R)-2-((1E,3R)-3-Hydroxyoct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635309-89-6P, 4-[2-[(2S)-2-((1E,3S)-3-Hydroxyoct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635309-90-9P, 4-[2-[(2S)-2-((1E,3R)-3-Hydroxyoct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635309-93-2P 635309-94-3P 635309-95-4P, 4-[2-[(2R)-2-[(1E,3R)-3-Hydroxy-3-(1-phenylcyclopropyl]prop-1-enyl]-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635309-96-5P, 4-[2-[(2R)-2-[(1E,3S)-3-Hydroxy-3-(1-phenylcyclopropyl]prop-1-enyl]-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635309-98-7P, 4-[2-[(2R)-2-[(1E,3S)-3-Hydroxy-4-(3-chlorophenyl)but-1-enyl]-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-03-1P, 4-[2-[(2R)-2-((1E,3S)-3-Hydroxynon-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-10-0P 635310-11-1P 635310-13-3P, 4-[2-[(2R)-2-((1E,3R)-3-Hydroxy-4-methyl-4-phenylpent-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-14-4P, 4-[2-[(2R)-2-((1E,3S)-3-Hydroxy-4-methyl-4-phenylpent-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-15-5P, 4-[2-[(2R)-2-((1E,3S)-3-Hydroxyhept-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-21-3P 635310-22-4P 635310-25-7P 635310-26-8P 635310-31-5P 635310-33-7P 635310-37-1P, 4-[2-[(2R)-2-[(E,3R)-3-Hydroxy-3-[1-(4-methylphenyl)cyclopentyl]prop-1-enyl]-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-38-2P 635310-41-7P 635310-42-8P 635310-45-1P, 4-[2-[(2R)-2-[(1E,3R)-3-Hydroxy-3-(1-phenylcyclopentyl)prop-1-enyl]-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-46-2P, 4-[2-[(2R)-2-[(1E,3S)-3-Hydroxy-3-(1-phenylcyclopentyl)prop-1-enyl]-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-47-3P, 4-[2-[(2R)-2-((1E,3S)-3-Hydroxy-6-methoxyhex-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-49-5P, 4-[2-[(2R)-2-((1E,3S)-3-Hydroxy-4-cyclohexylbut-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-51-9P, 4-[2-[(2R)-2-((1E,3S)-3-Hydroxy-4-phenylbut-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-54-2P, 4-[2-[(2R)-2-((1E,3S)-3-Hydroxyoct-1-en-7-ynyl)-5-oxopyrrolidin-1-

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
yl]ethyl]benzoic acid 635310-57-5P, 4-[2-[(2R)-2-((1E,3S)-5,5-Dimethyl-3-hydroxyhex-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-59-7P, 4-[2-[(2R)-2-((1E,3S)-5-Methyl-3-hydroxyhex-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-61-1P, 4-[2-[(2R)-2-((1E,3S)-7-Chloro-3-hydroxyhept-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-64-4P, 4-[2-[(2R)-2-((1E,3S)-3-Hydroxyoct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzamide 635310-68-8P, 4-[2-[(2R)-2-((1E,3S,7R)-3,7-Dihydroxyoct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-71-3P, 4-[2-[(2R)-2-((1E,3R,7R)-3,7-Dihydroxyoct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-76-8P, 4-[2-[(2R)-2-((1E,3S,7S)-3,7-Dihydroxyoct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-77-9P, 4-[2-[(2R)-2-((1E,3R,7S)-3,7-Dihydroxyoct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-82-6P 635310-83-7P 635310-84-8P, 4-[2-[(2R)-2-[(1E,3R)-3-Hydroxy-3-(1-propylcyclobutyl)prop-1-enyl]-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-85-9P, 4-[2-[(2R)-2-[(1E,3S)-3-Hydroxy-3-(1-propylcyclobutyl)prop-1-enyl]-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-86-0P 635310-87-1P, 4-[2-[(2R)-2-[(1E,3R)-3-Hydroxy-3-[1-(2-phenylethyl)cyclobutyl]prop-1-enyl]-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-88-2P, 4-[2-[(2R)-2-[(1E,3S)-3-Hydroxy-3-[1-(2-phenylethyl)cyclobutyl]prop-1-enyl]-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-89-3P, 4-[2-[(2R)-2-((1E,3S)-3-Hydroxy-5-phenylpent-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-91-7P 635310-92-8P 635310-93-9P 635310-94-0P 635310-95-1P,

4-[2-[(2R)-2-((1E,3S)-4-Cyclopropyl-3-hydroxybut-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-96-2P, 4-[2-[(2R)-2-((1E,3R)-4-Cyclopropyl-3-hydroxybut-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-97-3P, 4-[2-[(2R)-2-((1E,3S)-4-Cyclopentyl-3-hydroxybut-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-98-4P,

4-[2-[(2R)-2-((1E,3R)-4-Cyclopentyl-3-hydroxybut-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635310-99-5P 635311-01-2P 635311-02-3P 635311-03-4P, 4-[2-[(2R)-2-((1E,3S)-3-Hydroxypent-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635311-04-5P, 4-[2-[(2R)-2-((1E,3S)-3-Hydroxyhex-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635311-05-6P,

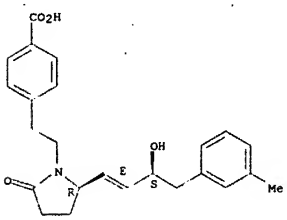
4-[2-[(5R)-2-Oxo-5-((1E,3S)-6,6,6-trifluoro-3-hydroxyhex-1-enyl]pyrrolidin-1-yl]ethyl]benzoic acid 635311-06-7P, 4-[2-[(2R)-2-((1E,3S)-3-Hydroxy-6-methylhept-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635311-07-8P, 4-[2-[(2R)-2-((1E,3S)-6-Cyclopropyl-3-hydroxyhex-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635311-09-0P 635311-10-3P, 4-[2-[(2R)-2-((1E,3R)-3-Hydroxy-4-phenoxybut-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635311-11-4P 635311-13-6P, 4-[2-[(2R)-2-((1E,3R)-3-Hydroxy-5-methoxypent-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635311-14-7P, 4-[2-[(2R)-2-((1E,3S)-3-Hydroxy-5-methoxypent-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635311-15-8P 635311-16-9P 635311-17-0P, 4-[2-[(2R)-2-((1E,3R)-5-Cyclopentyl-3-hydroxypent-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635311-19-2P, 4-[2-[(2R)-2-((1E,3R)-3-Hydroxy-7-methyloct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635311-21-6P, 4-[2-[(2R)-2-((1E,4S)-4-Hydroxyoct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635311-22-7P, 4-[2-[(2R)-2-[(1E,4R)-4-Hydroxy-4-(1-propylcyclobutyl)but-1-enyl]-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635311-23-8P 635311-24-9P 635311-25-0P,

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

4-[2-[(2R)-2-((1E,3S)-3-Hydroxy-4,4-dimethyloct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635311-26-1P, 4-[2-[(2S)-2-((1E,4S)-4-Hydroxy-4-ethyloct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635311-28-3P, 4-[2-[(2R)-2-((1E,3R)-3-Hydroxy-4,4-dimethyloct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635311-29-4P, 4-[2-[(2R)-2-((1E,3S)-3-Hydroxy-7-methyloct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid 635311-30-7P, 4-[2-[(2R)-2-((1E,3S)-5-Cyclopentyl-3-hydroxypent-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(EP4 agonist; prepn. of pyrrolidinones as prostaglandin EP4 agonists for treatment of preterm labor, dysmenorrhea, sexual dysfunction, bone loss, inflammation, and other disorders)

RN 494223-72-2 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-methylphenyl)-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

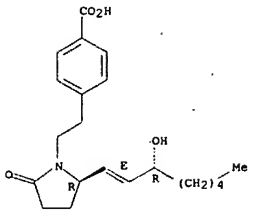
Absolute stereochemistry.
Double bond geometry as shown.



RN 635309-88-5 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

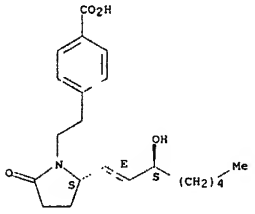
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635309-89-6 CAPLUS
CN Benzoic acid, 4-[2-[(2S)-2-[(1E,3S)-3-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

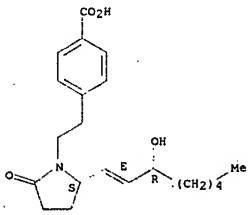
Absolute stereochemistry.
Double bond geometry as shown.



RN 635309-90-9 CAPLUS
CN Benzoic acid, 4-[2-[(2S)-2-[(1E,3R)-3-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

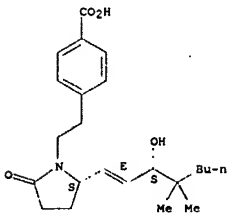
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635309-93-2 CAPLUS
CN Benzoic acid, 4-[2-[(2S)-2-[(1E,3S)-3-hydroxy-4,4-dimethyl-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

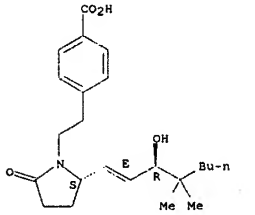
Absolute stereochemistry.
Double bond geometry as shown.



RN 635309-94-3 CAPLUS
CN Benzoic acid, 4-[2-[(2S)-2-[(1E,3R)-3-hydroxy-4,4-dimethyl-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

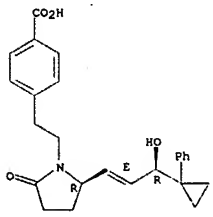
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635309-95-4 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-hydroxy-3-(1-phenylcyclopropyl)-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

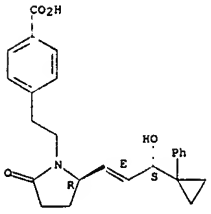
Absolute stereochemistry.
Double bond geometry as shown.



RN 635309-96-5 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-3-(1-phenylcyclopropyl)-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

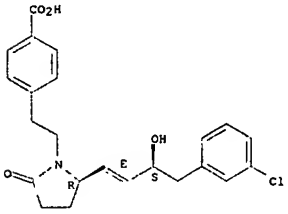
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635309-98-7 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-(3-chlorophenyl)-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

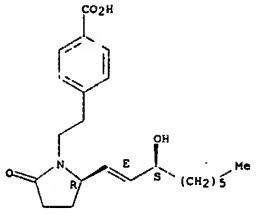
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-03-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-nonenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

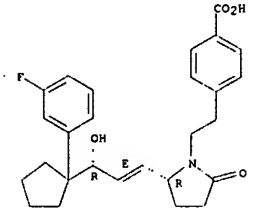
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-10-0 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-[1-(3-fluorophenyl)cyclopentyl]-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

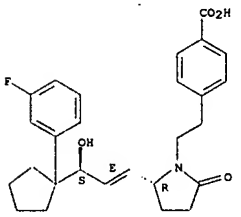
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-11-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-[1-(3-fluorophenyl)cyclopentyl]-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

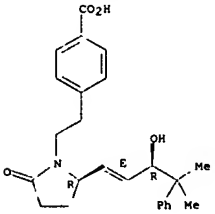
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-13-3 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-hydroxy-4-methyl-4-phenyl-1-pentenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

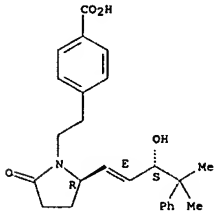
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-14-4 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-methyl-4-phenyl-1-pentenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

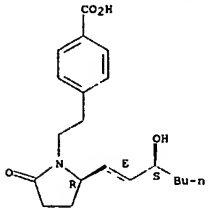
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-15-5 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-heptenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

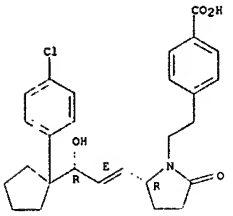
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-21-3 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-[1-(4-chlorophenyl)cyclopentyl]-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

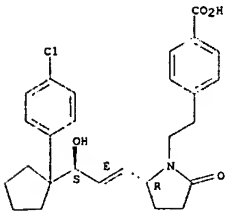
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-22-4 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-[1-(4-chlorophenyl)cyclopentyl]-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

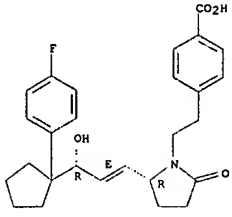
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-25-7 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-[1-(4-fluorophenyl)cyclopentyl]-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

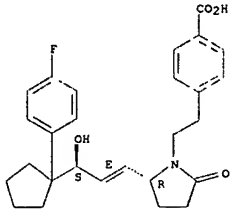
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-26-8 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-[1-(4-fluorophenyl)cyclopentyl]-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

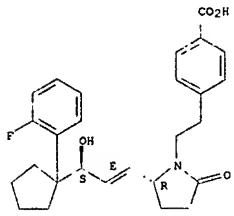
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-31-5 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-[1-(2-fluorophenyl)cyclopentyl]-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

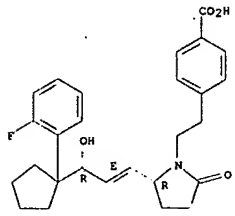
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-33-7 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-[1-(2-fluorophenyl)cyclopentyl]-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

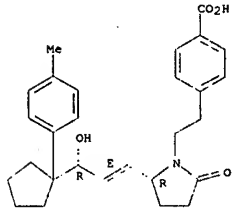
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-37-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-hydroxy-3-[1-(4-methylphenyl)cyclopentyl]-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

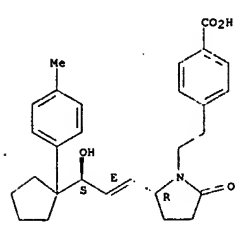
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-38-2 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-3-[1-(4-methylphenyl)cyclopentyl]-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

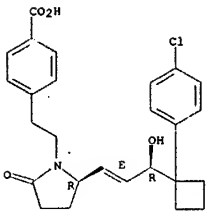
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-41-7 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-[1-(4-chlorophenyl)cyclobutyl]-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

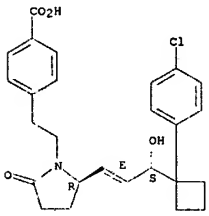
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-42-8 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-[1-(4-chlorophenyl)cyclobutyl]-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

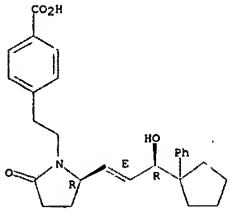
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-45-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-hydroxy-3-(1-phenylcyclopentyl)-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

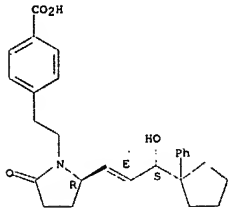
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-46-2 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-3-(1-phenylcyclopentyl)-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

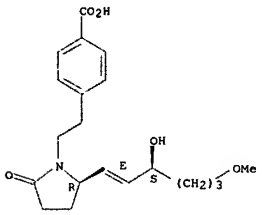
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-47-3 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-6-methoxy-1-hexenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

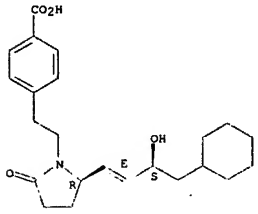
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-49-5 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-cyclohexyl-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

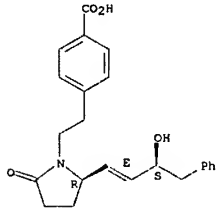
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-51-9 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

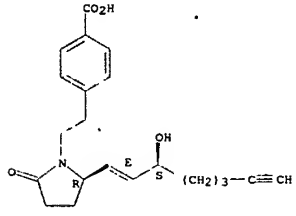
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-54-2 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-octen-7-ynyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

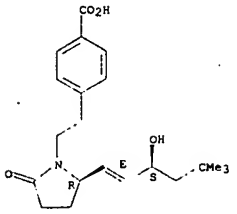
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-57-5 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-5,5-dimethyl-1-hexenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

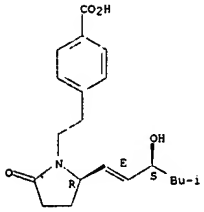
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-59-7 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-5-methyl-1-hexenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

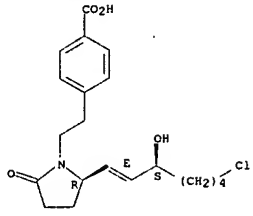
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-61-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-7-chloro-3-hydroxy-1-heptenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

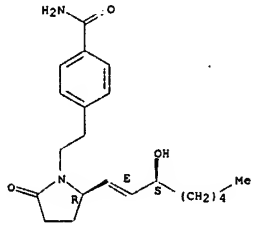
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-64-4 CAPLUS
CN Benzamide, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

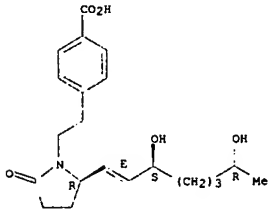
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-68-8 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S,7R)-3,7-dihydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

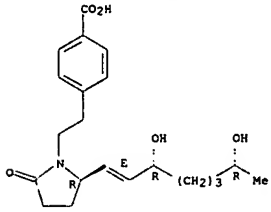
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-71-3 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R,7R)-3,7-dihydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

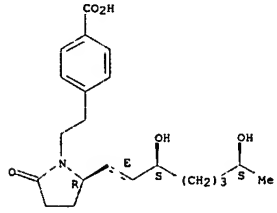
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-76-8 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S,7S)-3,7-dihydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

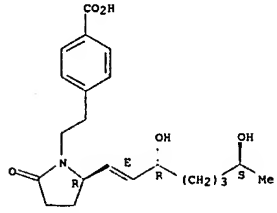
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-77-9 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R,7S)-3,7-dihydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

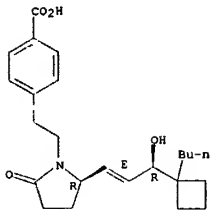
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-82-6 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-(1-butylcyclobutyl)-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

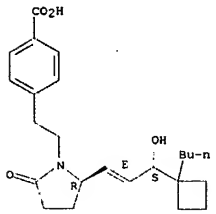
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-83-7 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-(1-butylcyclobutyl)-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

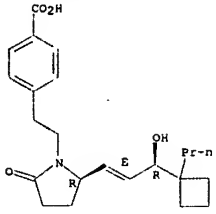
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-84-8 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-hydroxy-3-(1-propylcyclobutyl)-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

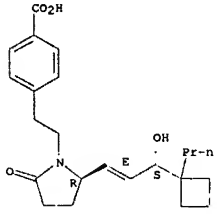
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-85-9 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-3-(1-propylcyclobutyl)-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

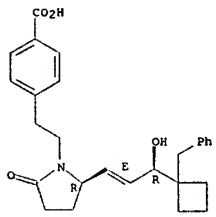
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-86-0 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-hydroxy-3-[1-(phenylmethyl)cyclobutyl]-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

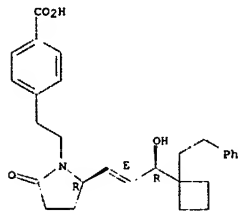
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-87-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-hydroxy-3-[1-(2-phenylethyl)cyclobutyl]-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

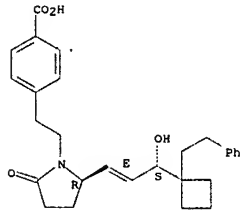
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-88-2 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-3-[1-(2-phenylethyl)cyclobutyl]-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

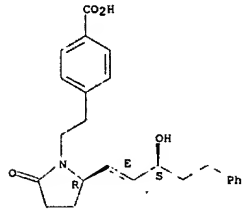
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-89-3 CAPLUS
CN Benzoic acid,
4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

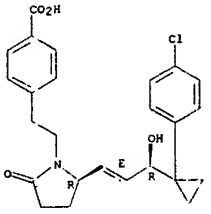
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-91-7 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-[1-(4-chlorophenyl)cyclopropyl]-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

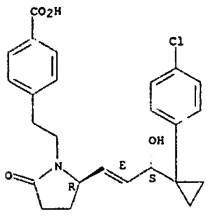
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-92-8 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-[1-(4-chlorophenyl)cyclopropyl]-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

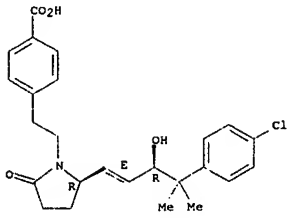
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-93-9 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-4-(4-chlorophenyl)-3-hydroxy-4-methyl-1-pentenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

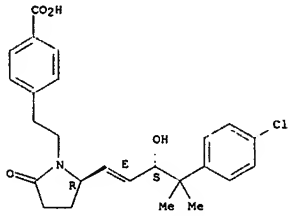
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-94-0 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-(4-chlorophenyl)-3-hydroxy-4-methyl-1-pentenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

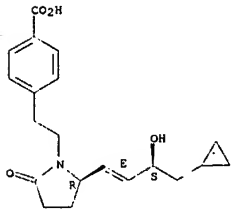
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-95-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-cyclopropyl-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

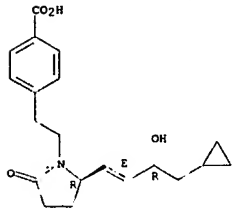
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-96-2 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-4-cyclopropyl-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

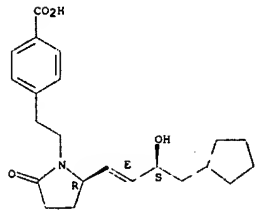
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-97-3 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-cyclopentyl-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

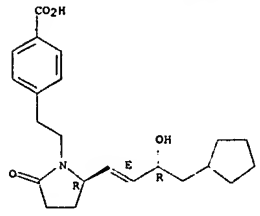
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-98-4 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-4-cyclopentyl-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

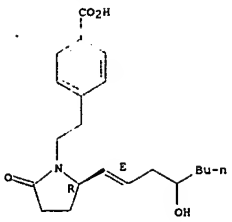
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-99-5 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E)-4-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

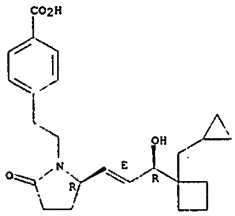
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635311-01-2 CAPLUS
CN Benzoic acid,
4-[2-[(2R)-2-[(1E,3R)-3-[1-(cyclopropylmethyl)cyclobutyl]-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

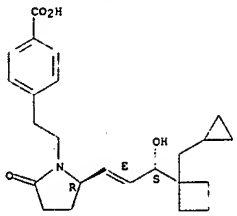
Absolute stereochemistry.
Double bond geometry as shown.



RN 635311-02-3 CAPLUS
CN Benzoic acid,
4-[2-[(2R)-2-[(1E,3S)-3-[1-(cyclopropylmethyl)cyclobutyl]-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

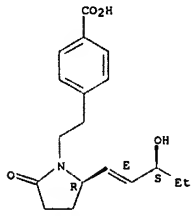
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635311-03-4 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-pentenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

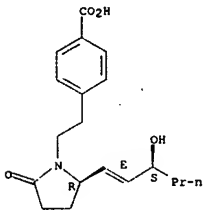
Absolute stereochemistry.
Double bond geometry as shown.



RN 635311-04-5 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-hexenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

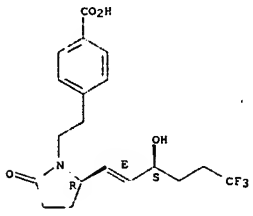
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635311-05-6 CAPLUS
CN Benzoic acid, 4-[2-[(5R)-2-oxo-5-[(1E,3S)-6,6,6-trifluoro-3-hydroxy-1-hexenyl]-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

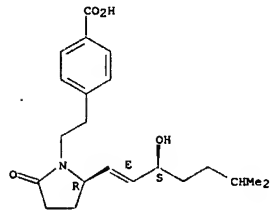
Absolute stereochemistry.
Double bond geometry as shown.



RN 635311-06-7 CAPLUS
CN Benzoic acid,
4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-6-methyl-1-heptenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

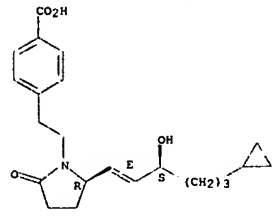
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635311-07-8 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-6-cyclopropyl-3-hydroxy-1-hexenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

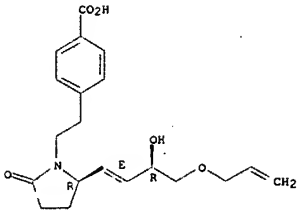
Absolute stereochemistry.
Double bond geometry as shown.



RN 635311-09-0 CAPLUS
CN Benzoic acid,
4-[2-[(2R)-2-[(1E,3R)-3-hydroxy-4-(2-propenyloxy)-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

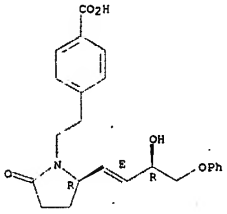
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635311-10-3 CAPLUS
CN Benzoic acid,
4-[2-[(2R)-2-[(1E,3R)-3-hydroxy-4-phenoxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

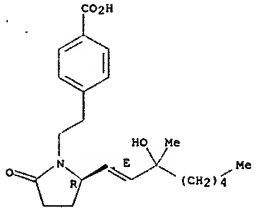
Absolute stereochemistry.
Double bond geometry as shown.



RN 635311-11-4 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E)-3-hydroxy-3-methyl-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

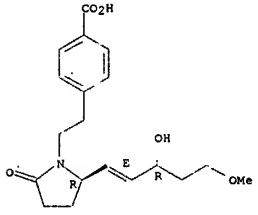
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635311-13-6 CAPLUS
CN Benzoic acid,
4-[2-[(2R)-2-[(1E,3R)-3-hydroxy-5-methoxy-1-pentenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

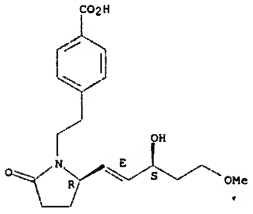
Absolute stereochemistry.
Double bond geometry as shown.



RN 635311-14-7 CAPLUS
CN Benzoic acid,
4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-5-methoxy-1-pentenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

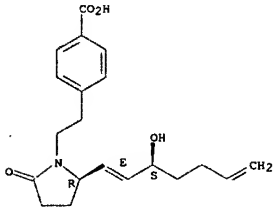
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635311-15-8 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1,6-heptadienyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

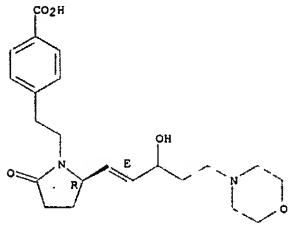
Absolute stereochemistry.
Double bond geometry as shown.



RN 635311-16-9 CAPLUS
CN Benzoic acid,
4-[2-[(2R)-2-[(1E)-3-hydroxy-5-(4-morpholinyl)-1-pentenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

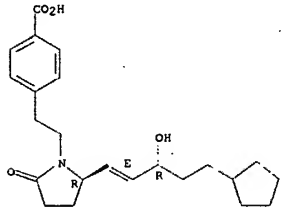
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635311-17-0 CAPLUS
CN Benzoic acid,
4-[2-[(2R)-2-[(1E,3R)-5-cyclopentyl-3-hydroxy-1-pentenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

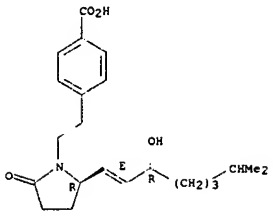
Absolute stereochemistry.
Double bond geometry as shown.



RN 635311-19-2 CAPLUS
CN Benzoic acid,
4-[2-[(2R)-2-[(1E,3R)-3-hydroxy-7-methyl-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

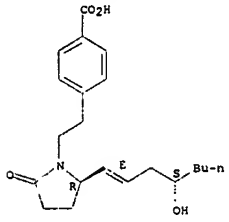
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635311-21-6 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,4S)-4-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

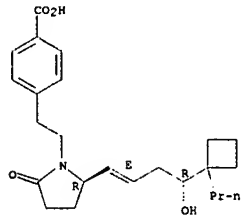
Absolute stereochemistry.
Double bond geometry as shown.



RN 635311-22-7 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,4R)-4-hydroxy-4-(1-propylcyclobutyl)-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

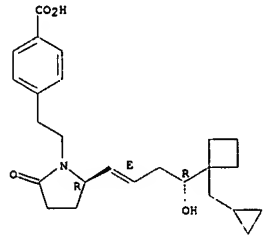
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635311-23-8 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,4R)-4-[1-(cyclopropylmethyl)cyclobutyl]-4-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

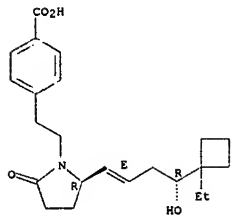
Absolute stereochemistry.
Double bond geometry as shown.



RN 635311-24-9 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,4R)-4-(1-ethylcyclobutyl)-4-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

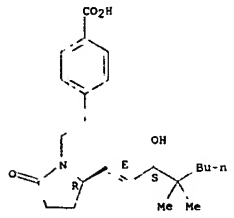
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635311-25-0 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4,4-dimethyl-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

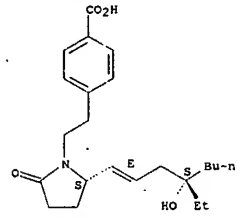
Absolute stereochemistry.
Double bond geometry as shown.



RN 635311-26-1 CAPLUS
CN Benzoic acid, 4-[2-[(2S)-2-[(1E,4S)-4-ethyl-4-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

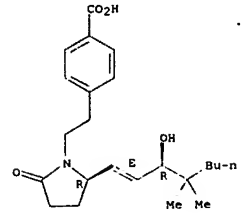
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635311-28-3 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R)-3-hydroxy-4,4-dimethyl-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

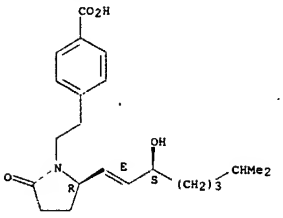
Absolute stereochemistry.
Double bond geometry as shown.



RN 635311-29-4 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-7-methyl-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

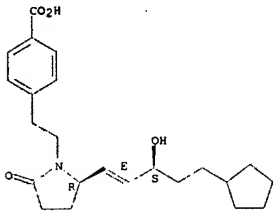
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635311-30-7 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-5-cyclopentyl-3-hydroxy-1-pentenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

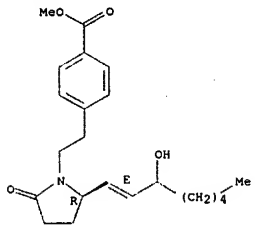


IT 635309-87-4P 635310-02-0P, Methyl 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-chlorophenyl)but-1-enyl]-5-oxopyrrolidin-1-yl]ethyl]benzoate 635310-06-4P, Methyl 4-[2-[(2R)-2-((1E,3S)-3-hydroxynon-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoate 635310-18-8P, Methyl 4-[2-[(2R)-2-((1E,3S)-3-hydroxyhept-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoate 635310-29-1P 635310-53-1P, Methyl 4-[2-[(2R)-2-((1E,3S)-3-hydroxy-4-phenylbut-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoate 635310-70-2P, Methyl 4-[2-[(2R)-2-((1E,3S,7R)-3,7-dihydroxyoct-1-enyl)-5-oxopyrrolidin-1-yl]ethyl]benzoate 635310-72-4P, Methyl 4-[2-[(2R)-2-((1E,3R,7R)-3,7-dihydroxyoct-1-enyl]-5-oxopyrrolidin-1-yl]ethyl]benzoate 635310-75-7P 635311-00-1P 635311-12-5P

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of pyrrolidinones as prostaglandin EP4 agonists for treatment of preterm labor, dysmenorrhea, sexual dysfunction, bone loss, inflammation, and other disorders)

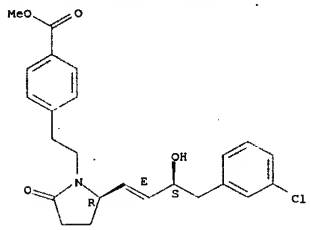
RN 635309-87-4 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E)-3-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-02-0 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-(3-chlorophenyl)-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

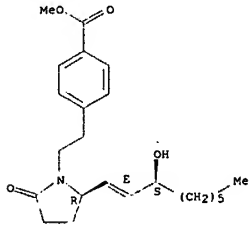
Absolute stereochemistry.
Double bond geometry as shown.



L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

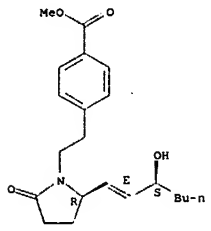
RN 635310-06-4 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-nonenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-18-8 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-heptenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

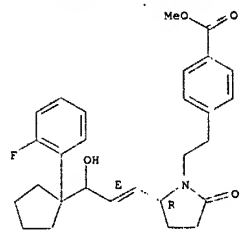
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-29-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E)-3-[1-(2-fluorophenyl)cyclopentyl]-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

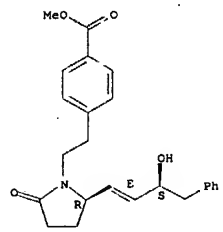
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-53-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

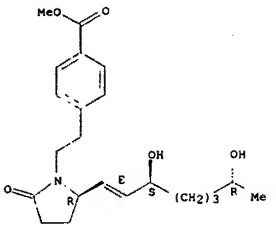
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-70-2 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S,7R)-3,7-dihydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

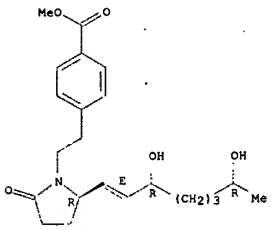
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635310-72-4 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3R,7R)-3,7-dihydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

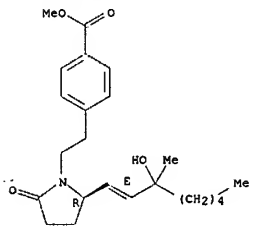
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-75-7 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,7S)-3,7-dihydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

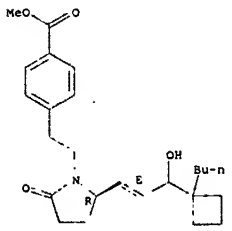
L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



IT 635310-65-5 635310-79-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrrolidinones as prostaglandin EP4 agonists for treatment
of preterm labor, dysmenorrhea, sexual dysfunction, bone loss, inflammation, and other disorders)

RN 635310-65-5 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E)-3-(1-butylcyclobutyl)-3-hydroxy-1-propenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

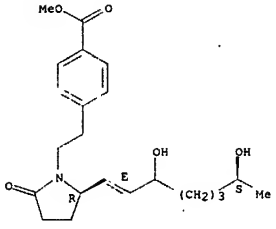
Absolute stereochemistry.
Double bond geometry as shown.



RN 635310-79-1 CAPLUS
CN Benzoic acid,
4-[2-[(2R)-2-[(1E)-3-hydroxy-4-methyl-4-phenyl-1-pentenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

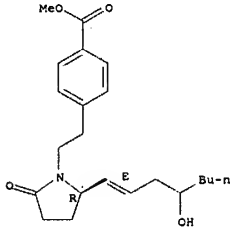
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 635311-00-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E)-4-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

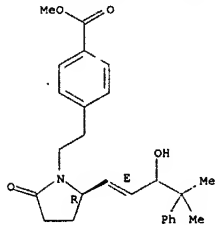
Absolute stereochemistry.
Double bond geometry as shown.



RN 635311-12-5 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E)-3-hydroxy-3-methyl-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:719446 CAPLUS
DOCUMENT NUMBER: 139:245813
TITLE: Preparation of 8-azaprostaglandin derivatives as EP2 and EP4 receptor agonists
INVENTOR(S): Tani, Kousuke; Kobayashi, Kaoru; Maruyama, Toru; Kambe, Tohru; Ogawa, Mikio; Shiroya, Tsutomu
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 436 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074483	A1	20030912	WO 2003-JP2478	20030304
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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CA 2477715	AA	20030912	CA 2003-2477715	20030304
AU 2003211574	A1	20030916	AU 2003-211574	20030304
EP 1481976	A1	20041201	EP 2003-743585	20030304
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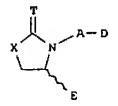
BR 2003008166	A	20050118	BR 2003-8166	20030304
US 2005124577	A1	20050609	US 2003-506536	20030304
CN 1653046	A	20050810	CN 2003-810251	20030304
NZ 535024	A	20061027	NZ 2003-535024	20030304
ZA 2004007034	A	20050309	ZA 2004-7034	20040902
NO 2004003702	A	20041203	NO 2004-3702	20040903
PRIORITY APPLN. INFO.:			JP 2002-58487 A	20020305
			JP 2002-216567 A	20020725
			JP 2003-13447 A	20030122
			WO 2003-JP2478 W	20030304

OTHER SOURCE(S): MARPAT 139:245813
GI

9/12/03 X

L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



I

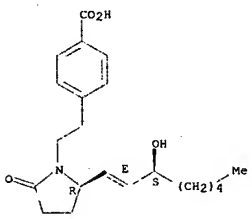
AB The title compds. I [T = O, etc.; X = CH2, etc.; A = alkylene, etc.; D = CO2H, etc.; E = U1U2U3, etc.; U1 = alkylene, etc.; U2 = CH2, etc.; U3 = (un)substituted alkyl, etc.] are prepared I are useful in preventing and/or treating immune diseases, allergic diseases, nerve cell death, premature birth, misbirth, baldness, retinal neuropathy such as glaucoma, erectile dysfunction, arthritis, pulmonary injury, pulmonary fibrosis, pulmonary emphysema, bronchitis, chronic obstructive pulmonary disease, hepatic injury, acute hepatitis, cirrhosis, shock, nephritis, renal insufficiency, circulatory diseases, systemic inflammatory response syndrome, sepsis, Still's disease, Kawasaki's disease, burn, systemic granuloma, ulcerative colitis, Crohn's disease, hypercytokinemia at dialysis, multiorgan failure, bone diseases, etc. In an in vitro test for binding to the EP2 receptor, one compound of this invention showed the Ki value of 14 nM. Formulations are given.

IT 493036-24-1P 597570-90-6P 597571-07-8P
597571-48-7P 597571-52-3P 597571-65-8P
597571-92-1P 597571-93-2P 597572-07-1P
597572-87-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 8-azaprostaglandin derivs. as EP2 and EP4 receptor agonists)

RN 493036-24-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

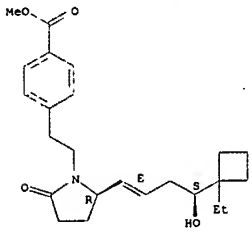
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 597570-90-6 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,4S)-4-(1-ethylcyclobutyl)-4-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

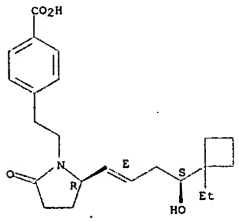
Absolute stereochemistry.
Double bond geometry as shown.



RN 597571-07-8 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,4S)-4-(1-ethylcyclobutyl)-4-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

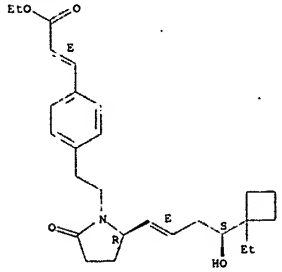
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 597571-48-7 CAPLUS
CN 2-Propenoic acid, 3-[4-[2-[(2R)-2-[(1E,4S)-4-(1-ethylcyclobutyl)-4-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]phenyl]-, ethyl ester, (2E)- (9CI) (CA INDEX NAME)

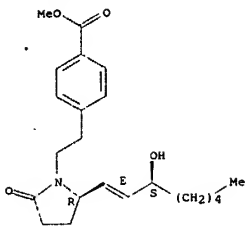
Absolute stereochemistry.
Double bond geometry as shown.



RN 597571-52-3 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

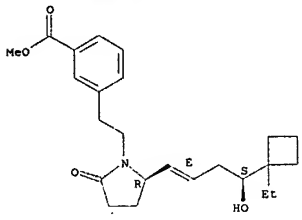
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 597571-65-8 CAPLUS
CN Benzoic acid, 3-[2-[(2R)-2-[(1E,4S)-4-(1-ethylcyclobutyl)-4-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

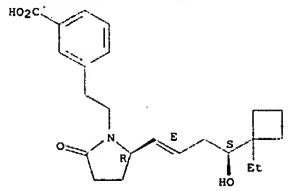
Absolute stereochemistry.
Double bond geometry as shown.



RN 597571-92-1 CAPLUS
CN Acetic acid, [4-[2-[(2R)-2-[(1E,4S)-4-(1-ethylcyclobutyl)-4-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]phenoxy]- (9CI) (CA INDEX NAME)

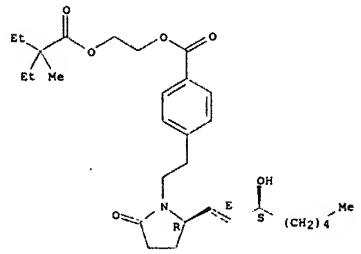
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



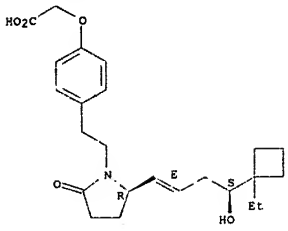
RN 597572-87-7 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, 2-(2-ethyl-2-methyl-1-oxobutoxy)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



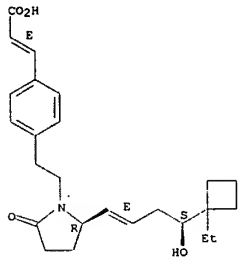
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 597571-93-2 CAPLUS
CN 2-Propenoic acid, 3-[4-[2-[(2R)-2-[(1E,4S)-4-(1-ethylcyclobutyl)-4-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 597572-07-1 CAPLUS
CN Benzoic acid, 3-[2-[(2R)-2-[(1E,4S)-4-(1-ethylcyclobutyl)-4-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:97322 CAPLUS
DOCUMENT NUMBER: 138:142493
TITLE: Remedies for diseases with bone mass loss having EP4 agonist as the active ingredient
INVENTOR(S): Maruyama, Toru; Kobayashi, Kaoru; Kambe, Tohru; Maruyama, Takayuki; Yoshida, Hideyuki; Nishiura, Akio; Abe, Nobutaka
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 474 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003009872	A1	20030206	WO 2002-JP7385	20020722
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2454584	AA	20030206	CA 2002-2454584	20020722
EP 1417975	A1	20040512	EP 2002-747707	20020722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011364	A	20040713	BR 2002-11364	20020722
ZA 2004000493	A	20050119	ZA 2004-493	20040122
US 2005020686	A1	20050127	US 2004-484500	20040122
NO 2004000331	A	20040323	NO 2004-331	20040123

PRIORITY APPLN. INFO.:
JP 2001-222148 A 20010723
JP 2001-239895 A 20010807
JP 2002-56449 A 20020301
WO 2002-JP7385 W 20020722

OTHER SOURCE(S): MARPAT 138:142493

AB Disclosed are drugs for topical administration which contain an EP4 agonist as the active ingredient for preventing and/or treating diseases in association with bone mass loss. The EP4 agonists typified by compds. with the prostaglandin skeleton have an effect of promoting osteogenesis. Thus, topical administration thereof is highly useful in preventing and/or treating diseases in association with bone mass loss, e.g., bone diseases such as primary osteoporosis, secondary osteoporosis, bone metastasis of cancer, hypercalcemia, Behcet's disease, bone loss and bone necrosis, postoperative osteogenesis, alternative therapy for bone transplantation.

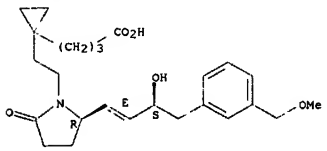
L3 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

A compd. (11α,15α,13E)-9-oxo-11,15-dihydroxy-16-(3-methoxymethylphenyl)-17,18,19,20-tetranor-5-thiaprost-13-enoic acid 2-nonanoyloxyethyl ester was prepd., and mixed with lactic acid-glycolic acid copolymer to obtain a microsphere. The obtained microsphere was administered to fracture bone part of a rat to examine the bone formation promoting effect.

IT 494221-67-9P 494223-72-2P 494223-77-7P
494224-01-0P 494224-02-1P 494224-03-2P
494224-04-3P 494224-05-4P 494224-06-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(remedies for diseases with bone mass loss containing prostaglandin EP4
receptor agonists as active ingredients)

RN 494221-67-9 CAPLUS
CN Cyclopropanebutanoic acid, 1-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-[3-(methoxymethyl)phenyl]-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

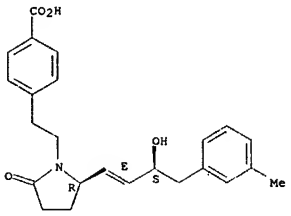
Absolute stereochemistry.
Double bond geometry as shown.



RN 494223-72-2 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-methylphenyl)-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

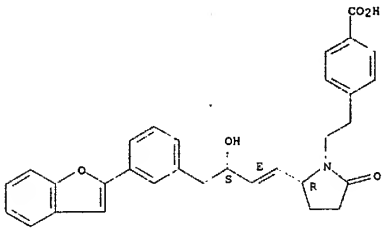
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 494223-77-7 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-[3-(2-benzofuranyl)phenyl]-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

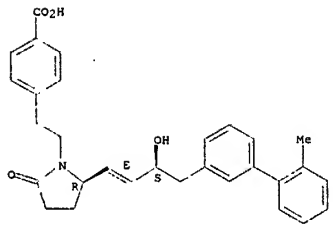
Absolute stereochemistry.
Double bond geometry as shown.



RN 494224-01-0 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(2'-methyl[1,1'-biphenyl]-3-yl)-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

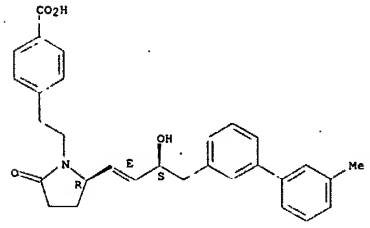
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 494224-02-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3'-methyl[1,1'-biphenyl]-3-yl)-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

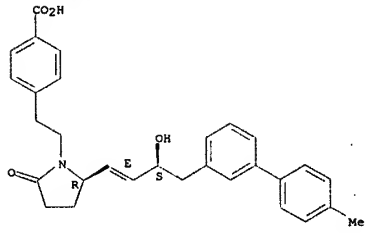
Absolute stereochemistry.
Double bond geometry as shown.



RN 494224-03-2 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(4'-methyl[1,1'-biphenyl]-3-yl)-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

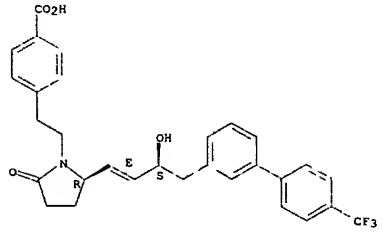
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 494224-04-3 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-[4'-(trifluoromethyl)[1,1'-biphenyl]-3-yl]-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

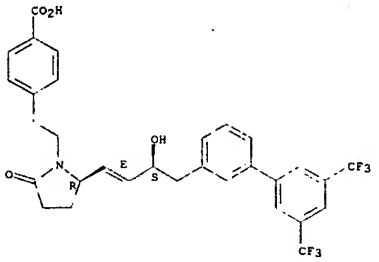
Absolute stereochemistry.
Double bond geometry as shown.



RN 494224-05-4 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-[3',5'-bis(trifluoromethyl)[1,1'-biphenyl]-3-yl]-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

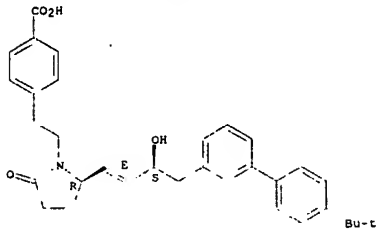
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 494224-06-5 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-4-[4'-(1,1-dimethylethyl)[1,1'-biphenyl]-3-yl]-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



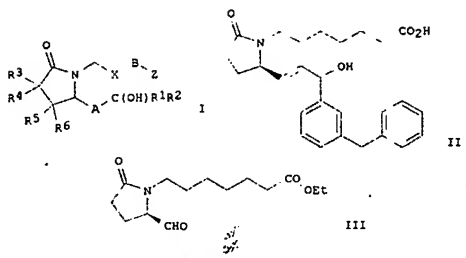
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:76747 CAPLUS
DOCUMENT NUMBER: 138:137086
TITLE: Preparation of pyrrolidine prostaglandin analogs for therapeutic use as EP4-type prostanoid receptor agonists
INVENTOR(S): Elworthy, Todd Richard; Mirzadegan, Taraneh; Roepel, Michael Garret; Smith, David Bernard; Walker, Keith Adrian Murray
PATENT ASSIGNEE(S): F. Hoffmann-La Roche AG, Switz.
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

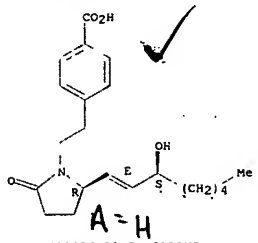
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008377	A1	20030130	WO 2002-EP7574	20020708
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2451392	AA	20030130	CA 2002-2451392	20020708
EP 1409455	A1	20040421	EP 2002-764647	20020708
EP 1409455	B1	20060104		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011201	A	20040713	BR 2002-11201	20020708
JP 2004521954	T2	20040722	JP 2003-513937	20020708
AT 315022	E	20060215	AT 2002-764647	20020708
ES 2254726	T3	20060616	ES 2002-2764647	20020708
CN 1863768	A	20061115	CN 2002-814091	20020708
US 2003130079	A1	20030626	US 2002-197353	20020716
US 6900336	B2	20050531		
PRIORITY APPLN. INFO.:			US 2001-305727P	P 20010716
			US 2002-371348P	P 20020410
			WO 2002-EP7574	W 20020708

OTHER SOURCE(S): MARPAT 138:137086
GI



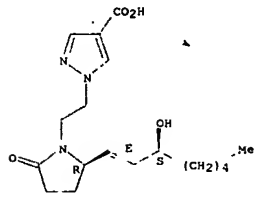
AB 8-Aza prostanoid analogs, such as I [R1 = alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl; R2-6 = H, alkyl, alkenyl, alkynyl; A = CH2CH2, CH:CH, CH:CHCH2; B = bond, aryl, heteroaryl; X = (CH2)1-6; Z = CH2OH, CO2H, tetrazol-5-yl, carboxy, carboxamido, phosphonate, etc.], were prepared as selective EP4-type prostanoid receptor agonists for pharmaceutical use in the treatment of bone disorders. Thus, azaprostanoid II was via a series of synthetic steps which included an olefination reaction of ester III with (MeO)2P(O)CH2COC6H4-3-CH2Ph. The prepared azaprostanoids were assayed for competitive binding of [3H]PGE2 to prostanoid types EP1, EP2, EP3, and EP4 receptors. Also, pharmaceutical formulations of the azaprostanoids were presented.
IT 493036-24-1P 493036-33-2P 493036-36-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidine prostaglandin analogs for therapeutic use as EP4 prostanoid receptor agonists for treatment of bone disorders)
RN 493036-24-1 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 493036-33-2 CAPLUS
CN 1H-Pyrazole-4-carboxylic acid, 1-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

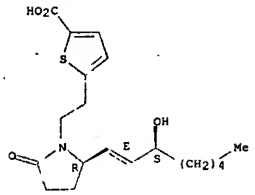
Absolute stereochemistry.
Double bond geometry as shown.



RN 493036-36-5 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

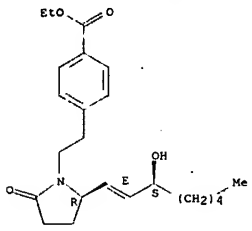
Absolute stereochemistry.
Double bond geometry as shown.

L3 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



IT 493036-28-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrrolidine prostaglandin analogs for therapeutic use as EP4
prostanoid receptor agonists for treatment of bone disorders)
RN 493036-28-5 CAPLUS
CN Benzoic acid, 4-[2-[(2R)-2-[(1E,3S)-3-hydroxy-1-octenyl]-5-oxo-1-pyrrolidinyl]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT